

chain nodes :

1 2 3 4 5 6 8 11

chain bonds :

1-2 1-6 2-3 2-11 3-4 4-5 5-8

exact/norm bonds :

2-3 2-11 3-4 4-5 5-8

exact bonds :

1-2 1-6

G1:O,S

Match level :

1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:Atom 8:CLASS 11:CLASS

Generic attributes :

6:

Saturation : Unsaturated

10/612014

=> s l1

SAMPLE SEARCH INITIATED 17:34:08 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 178 TO ITERATE

100.0% PROCESSED 178 ITERATIONS 2 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 2760 TO 4360  
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 17:34:23 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 3888 TO ITERATE

100.0% PROCESSED 3888 ITERATIONS 21 ANSWERS  
SEARCH TIME: 00.00.01

L3 21 SEA SSS FUL L1

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST  | 155.84           | 156.05        |

FILE 'CAPLUS' ENTERED AT 17:34:33 ON 16 DEC 2004  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1907 - 16 Dec 2004 VOL 141 ISS 25  
FILE LAST UPDATED: 15 Dec 2004 (20041215/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

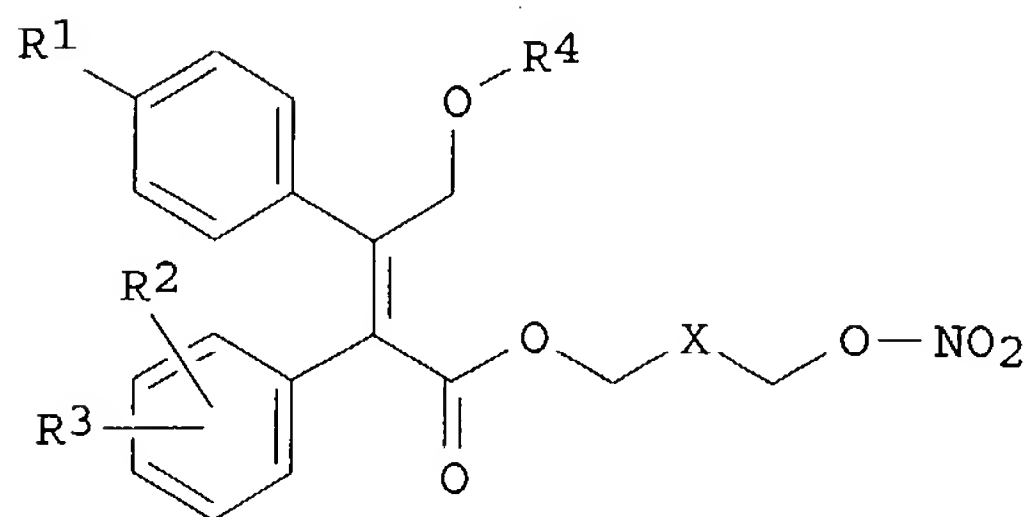
L4 14 L3

=> d l4 1-14 bib abs hitstr

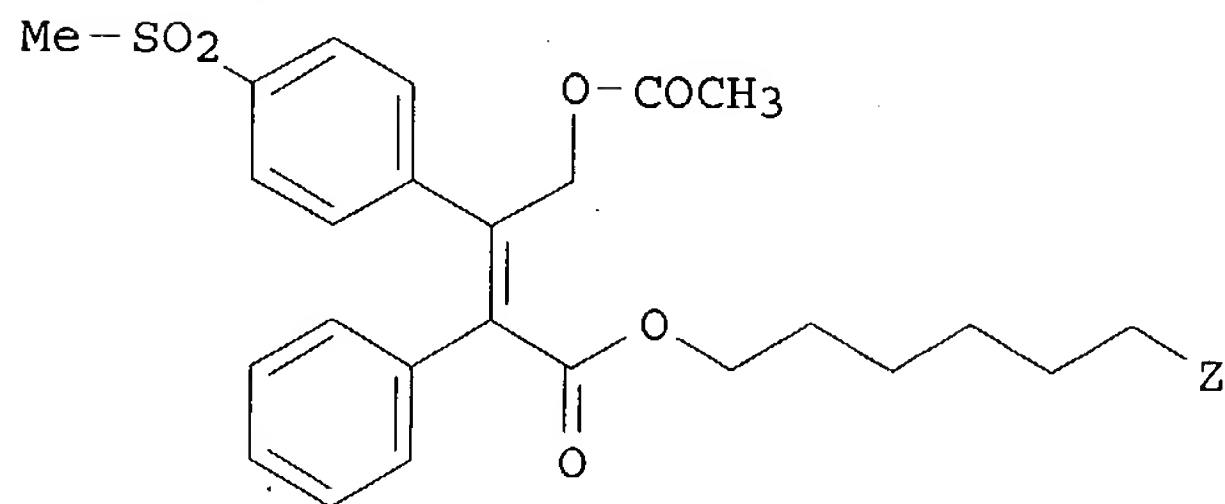
10/612014

L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:739958 CAPLUS  
DN 141:260542  
TI Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones  
as selective cyclooxygenase-2 inhibitors  
IN Berthelette, Carl; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin  
PA Can.  
SO U.S. Pat. Appl. Publ., 19 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | US 2004176331   | A1   | 20040909 | US 2004-790288  | 20040301 |
|      | WO 2004103955   | A1   | 20041202 | WO 2004-CA314   | 20040301 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
|      | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| PRAI | US 2003-452124P   | P    | 20030305 |                 |          |
| OS   | MARPAT 141:260542   |      |          |                 |          |
| GI   |   |      |          |                 |          |



I



II

AB Title compds. I [X = (CH<sub>2</sub>)<sub>n</sub>; n = 3-6; R<sub>1</sub> = SO<sub>2</sub>Me, SO<sub>2</sub>NH<sub>2</sub>, SO<sub>2</sub>NHCOCF<sub>3</sub>, etc.; R<sub>2</sub>, R<sub>3</sub> = H, halo, alkoxy, etc.; R<sub>4</sub> = CO-alkyl, CO(CH<sub>2</sub>)<sub>m</sub>NR<sub>5</sub>R<sub>6</sub>; m = 1-4; R<sub>5</sub>, R<sub>6</sub> = H, halo-substituted alkyl] and their pharmaceutically

10/612014

acceptable salts were prepared. For example, O-alkylation of AgNO<sub>3</sub> by bromide II (Z = Br), e.g., prepared from Rofecoxib in 6-steps, afforded nitrooxyhexyl II (Z = -ONO<sub>2</sub>). In human blood PGE<sub>2</sub> inhibition production assays, nitrooxyhexyl II (Z = -ONO<sub>2</sub>) exhibited an IC<sub>50</sub> value of 0.22 μM. Of note, the "unconverted prodrugs" of compds. I are inactive inhibitors of COX-1 and COX-2 activity. Compds. I are claimed useful for the treatment of cyclooxygenase-2 mediated diseases or conditions.

IT 754242-01-8P

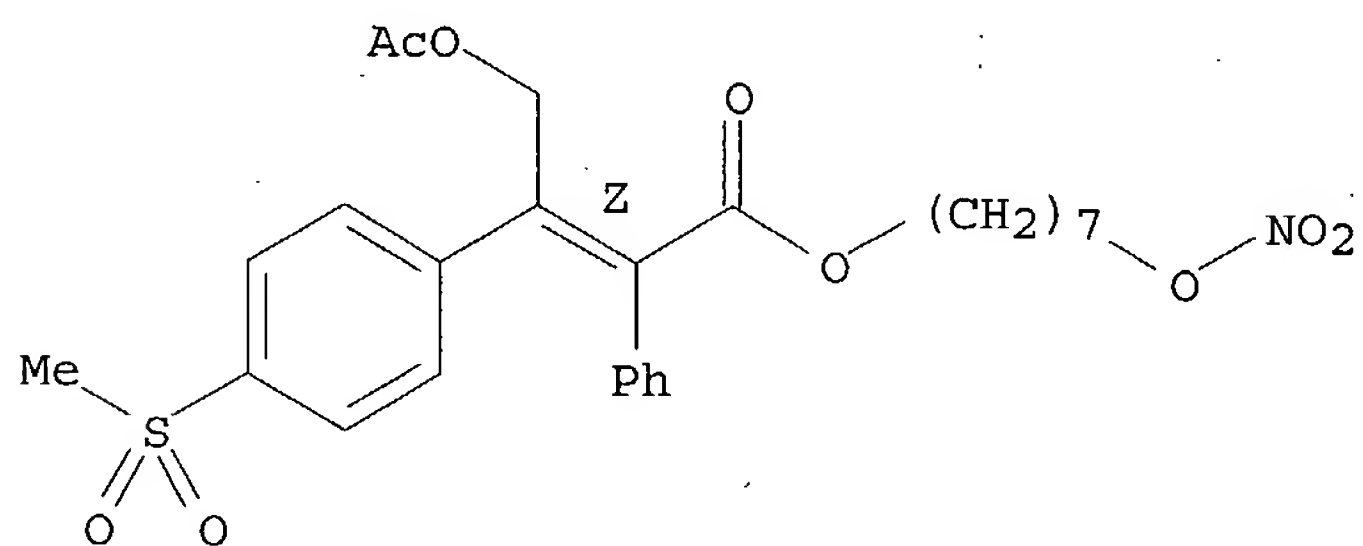
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitric oxide releasing prodrugs of diarylfuranones as selective COX-2 inhibitors)

RN 754242-01-8 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -[2-(acetyloxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 7-(nitrooxy)heptyl ester, ( $\alpha$ Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.





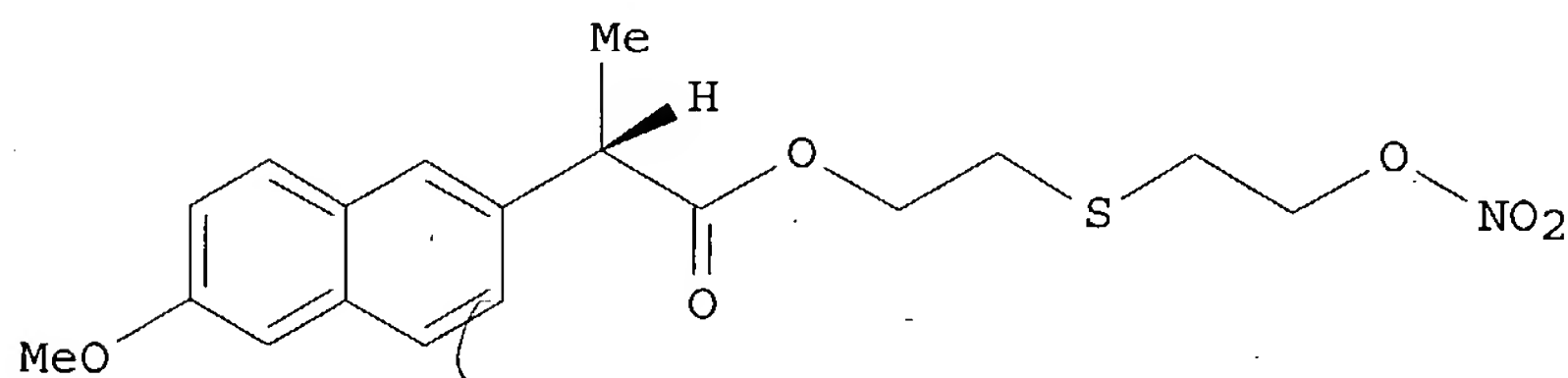
10/612014

10/612014

L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:41217 CAPLUS  
DN 140:111135  
TI Preparation of nitrosated nonsteroidal antiinflammatory compounds  
IN Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Khanapure, Subhash P.; Letts, Gordon L.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.; Stevenson, Cheri A.; Wey, Shiow-Jyi  
PA Nitromed, Inc., USA  
SO PCT Int. Appl., 145 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

Apps

|      | PATENT NO.        | KIND   | DATE     | APPLICATION NO. | DATE     |
|------|-------------------|--|----------|-----------------|----------|
| PI   | WO 2004004648     | A2   | 20040115 | WO 2003-US21026 | 20030703 |
|      | WO 2004004648     | A3   | 20041028 |                 |          |
|      | W:                | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |          |                 |          |
|      | RW:               | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
|      | US 2004024057     | A1   | 20040205 | US 2003-612014  | 20030703 |
| PRAI | US 2002-393111P   | P  | 20020703 |                 |          |
|      | US 2002-397979P   | P  | 20020724 |                 |          |
|      | US 2002-418353P   | P  | 20021016 |                 |          |
|      | US 2003-449798P   | P  | 20030226 |                 |          |
|      | US 2003-456182P   | P  | 20030321 |                 |          |
| OS   | MARPAT 140:111135 |  |          |                 |          |
| GI   |                   |  |          |                 |          |



II

AB Title compds. R<sub>n</sub>R<sub>m</sub>HC-CO-X [R<sub>m</sub> = H, alkyl; R<sub>n</sub> = 4-((thiophen-2-yl)carbonyl)phenyl, 3-(benzoyl)phenyl, etc.; X = Y-alkyl-aryl, etc.; Y = O, S; I] are prepared For instance, naproxen is coupled to 2,2'-thiodiethanol (CH<sub>2</sub>Cl<sub>2</sub>, DMAP, EDCI) and treated with Ac<sub>2</sub>O/HNO<sub>3</sub> at 0° to give II. I are nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) used alone or are combined with one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase. The invention provides methods for treating inflammation, pain, fever, gastrointestinal disorders, etc.

IT 646509-75-3P, 2-[[N-[2-(Nitrooxy)ethyl]carbamoyl]oxy]ethyl

10/612014

(2S)-2-(6-methoxy-2-naphthyl)propanoate 646509-99-1P,  
[N-Methyl-N-[[[2-(nitrooxy)ethyl]oxy]carbonyl]methyl]carbamoyl]methyl  
(2S)-2-(6-methoxy-2-naphthyl)propanoate 646510-05-6P,  
[N-Methyl-N-[[[3-(nitrooxy)propyl]oxy]carbonyl]methyl]carbamoyl]methyl  
(2S)-2-(6-methoxy-2-naphthyl)propanoate 646510-09-0P,  
[N-Methyl-N-[N-[2-(nitrooxy)ethyl]carbamoyl]methyl]carbamoyl]methyl  
(2S)-2-(6-methoxy-2-naphthyl)propanoate 646510-17-0P,  
[[[2-[[2-(Nitrooxy)ethyl]sulfonyl]ethyl]oxy]carbonyl]methyl  
(2S)-2-(6-methoxy-2-naphthyl)propanoate 646510-88-5P,  
2-[[[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxy]ethyl 3-(nitrooxy)propyl  
ethane-1,2-dioate 646511-50-4P, [[2-[[2-  
(Nitrooxy)ethyl]sulfonyl]ethyl]oxy]carbonyl]methyl 2-(6-methoxy-2-  
naphthyl)propanoate

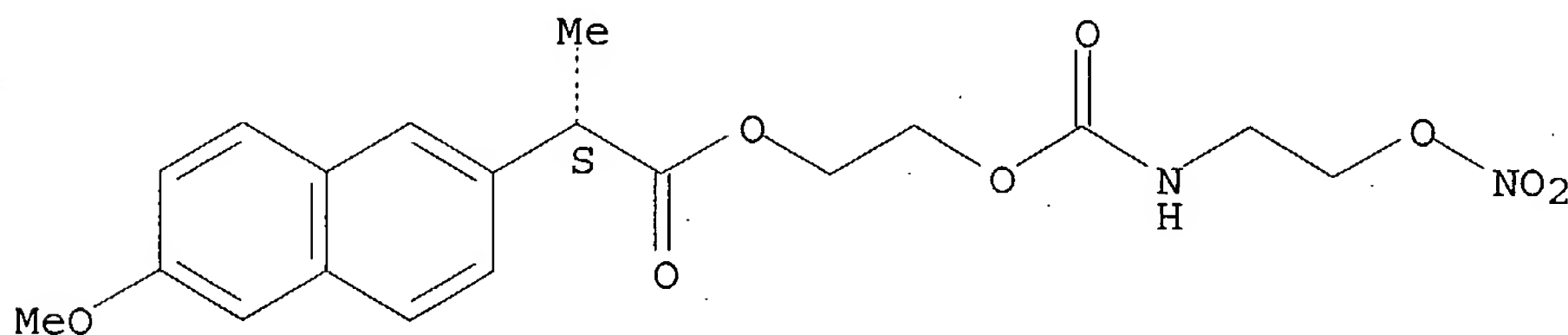
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of naproxen-derived nitrosated antiinflammatory compds.)

RN 646509-75-3 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 2-[[[2-  
(nitrooxy)ethyl]amino]carbonyl]oxy]ethyl ester, ( $\alpha$ S)- (9CI) (CA  
INDEX NAME)

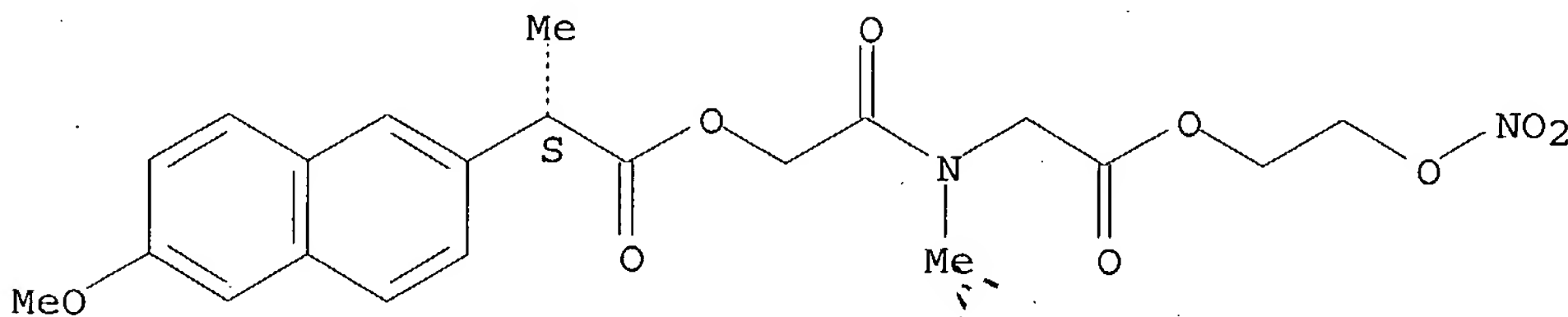
Absolute stereochemistry.



RN 646509-99-1 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 2-[methyl[2-[2-  
(nitrooxy)ethoxy]-2-oxoethyl]amino]-2-oxoethyl ester, ( $\alpha$ S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



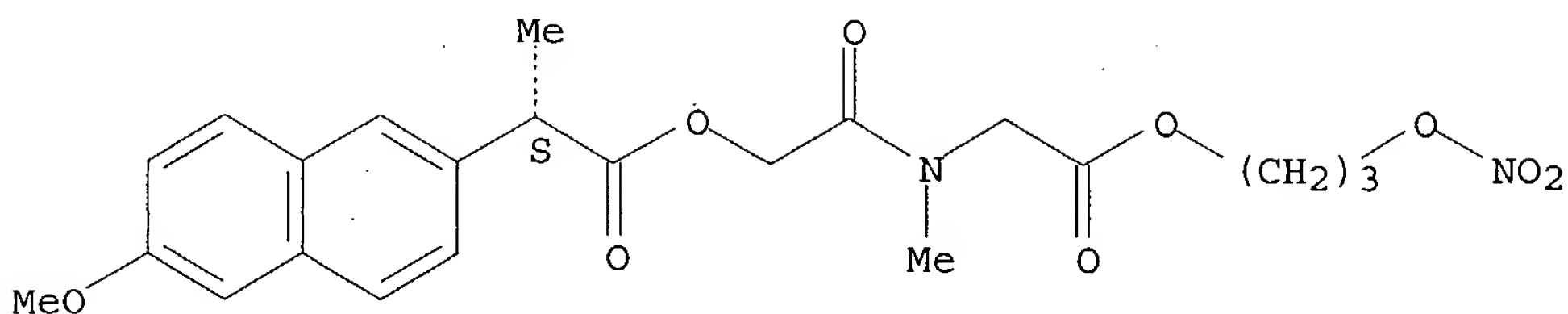
RN 646510-05-6 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 2-[methyl[2-[3-  
(nitrooxy)propoxy]-2-oxoethyl]amino]-2-oxoethyl ester, ( $\alpha$ S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



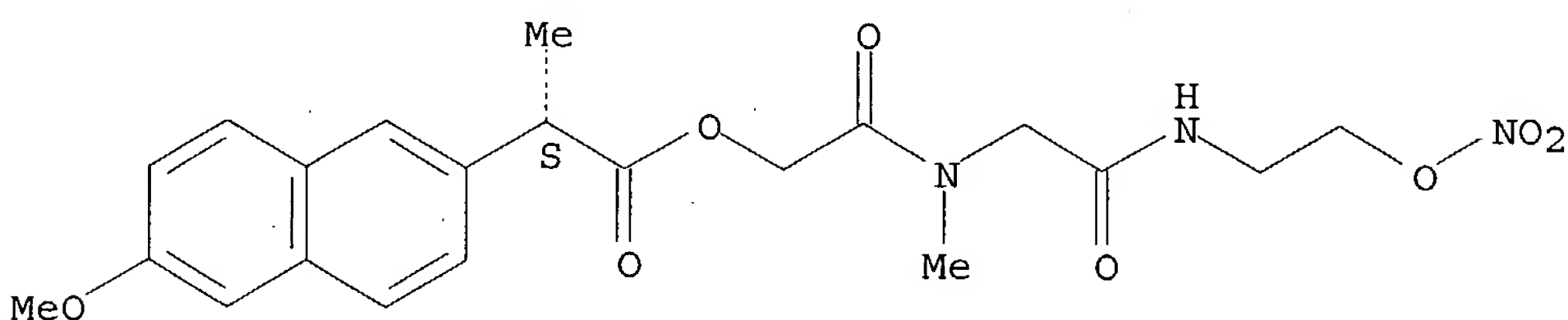
10/612014



RN 646510-09-0 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 2-[methyl[2-[[2-(nitrooxy)ethyl]amino]-2-oxoethyl]amino]-2-oxoethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

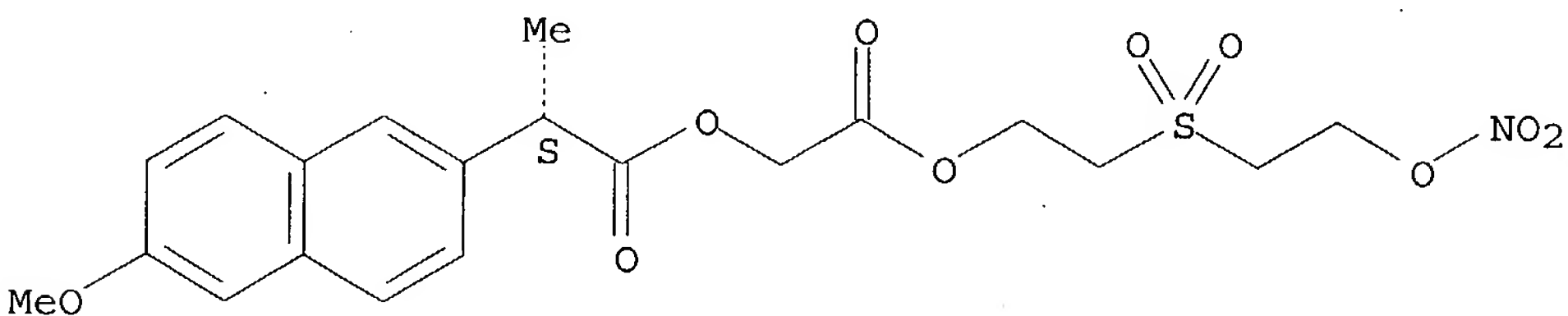
Absolute stereochemistry.



RN 646510-17-0 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 2-[2-[[2-(nitrooxy)ethyl]sulfonyl]ethoxy]-2-oxoethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

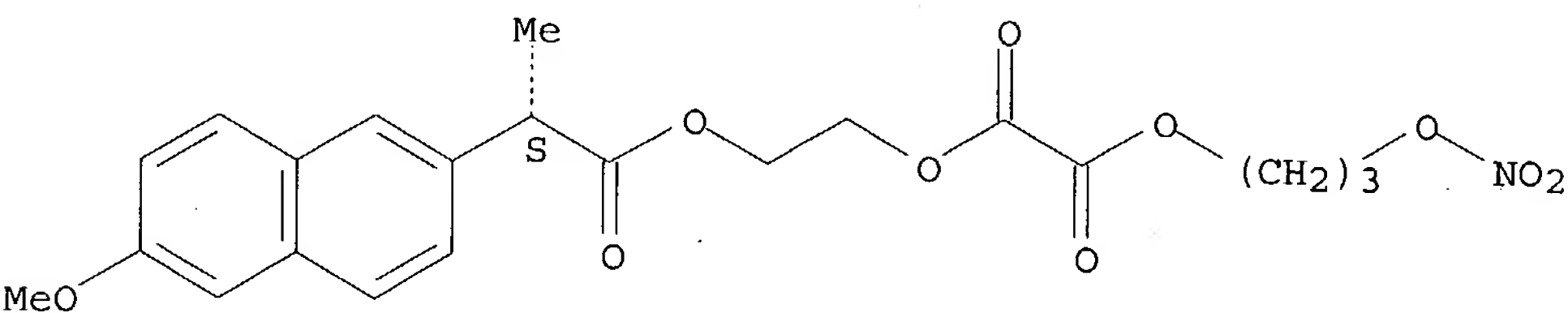
Absolute stereochemistry.



RN 646510-88-5 CAPLUS

CN Ethanedioic acid, 2-[(2S)-2-(6-methoxy-2-naphthalenyl)-1-oxopropoxy]ethyl 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

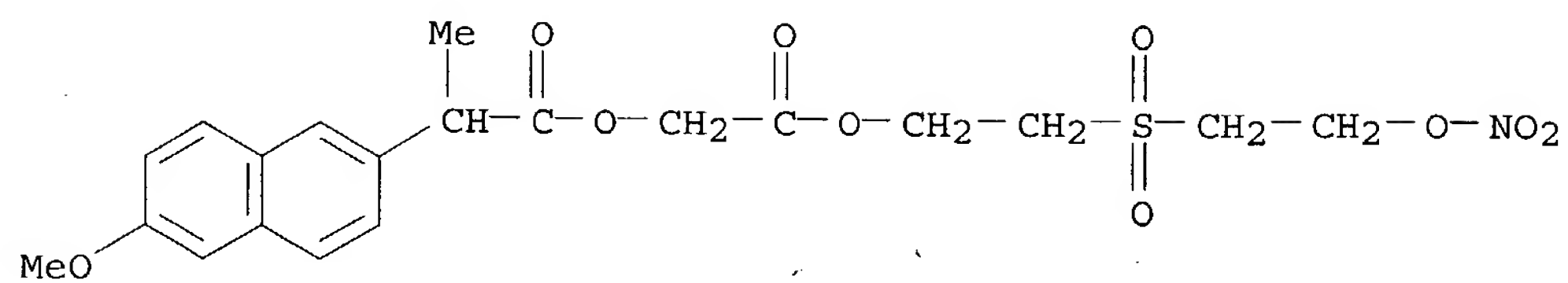
Absolute stereochemistry.



RN 646511-50-4 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 2-[2-[[2-(nitrooxy)ethyl]sulfonyl]ethoxy]-2-oxoethyl ester (9CI) (CA INDEX NAME)

10/612014



10/612014

L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:2684 CAPLUS  
DN 140:73178  
TI Nitroxy derivatives of non-steroidal anti-inflammatory compounds as  
selective inhibitors of cyclooxygenase-2 for the treatment of inflammation  
IN Del Soldato, Piero; Santus, Giancarlo  
PA Nicox S.A., Fr.  
SO PCT Int. Appl., 49 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2004000300   | A1   | 20031231 | WO 2003-EP6651  | 20030624 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| PRAI | IT 2002-MI1399  | A    | 20020625 |                 |          |

OS MARPAT 140:73178

AB The present invention relates to compds. able to inhibit selectively the enzyme cyclooxygenase-2 (COX-2) without inhibiting substantially the enzyme COX-1. Specifically, the present invention concerns nitroxy derivs. of non-steroidal anti-inflammatory compds., which are able to inhibit selectively the enzyme COX-2. The compds. of the invention are useful in the treatment and/or prophylaxis of inflammatory processes.

IT 302543-75-5 302543-76-6 302543-77-7

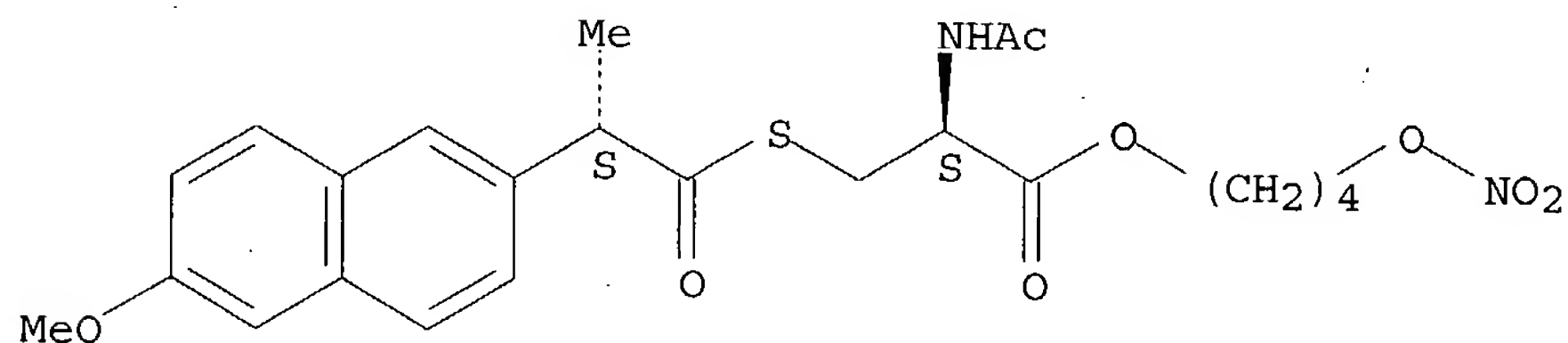
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

RN 302543-75-5 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

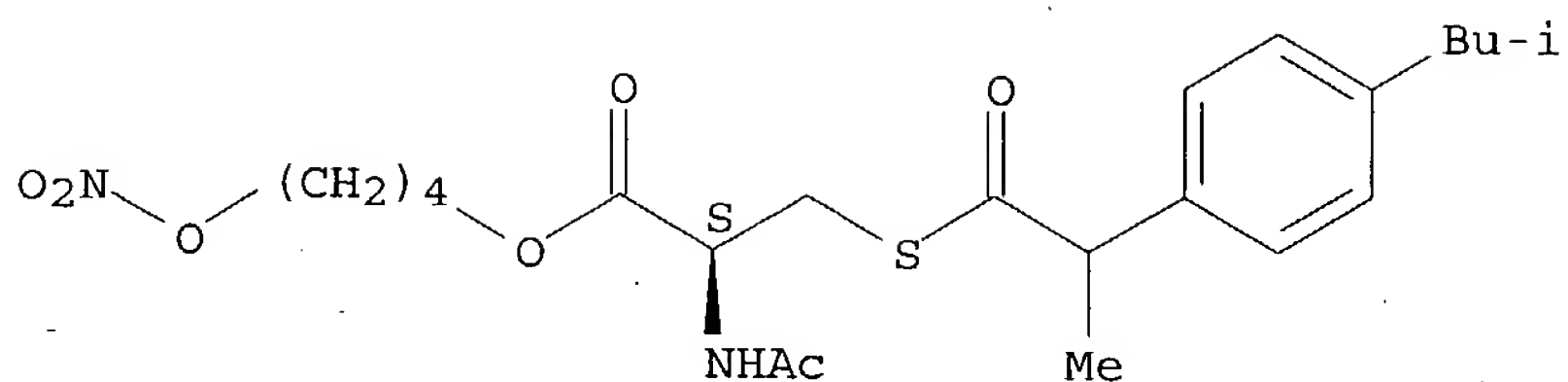


RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

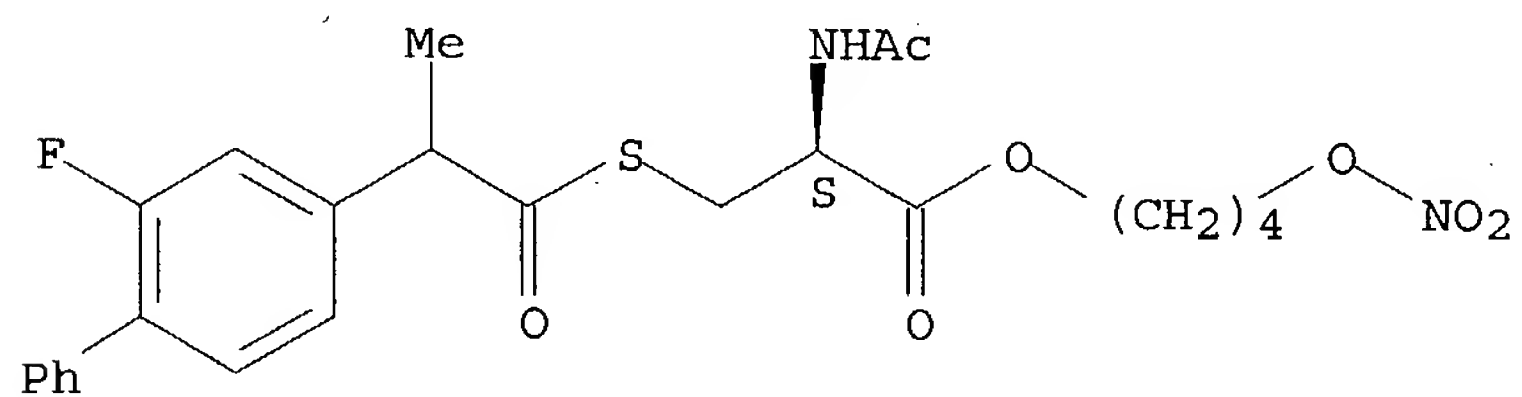
10/612014



RN 302543-77-7 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-fluoro- $\alpha$ -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

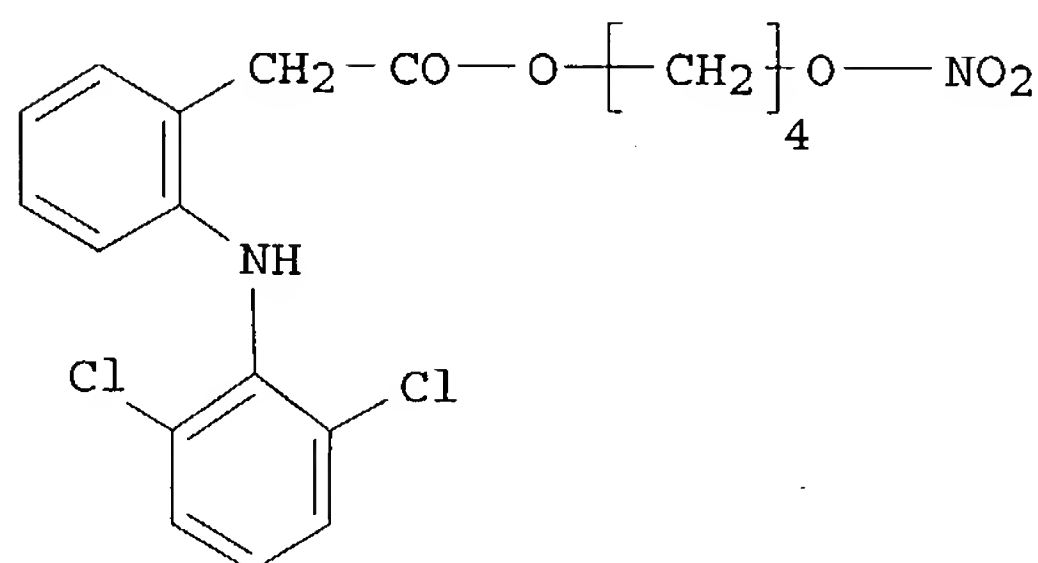


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/612014

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:2666 CAPLUS  
DN 140:65191  
TI Oral pharmaceutical liquid drugs containing nitrate ester NSAIDs having improved bioavailability  
IN Del Soldato, Piero; Santus, Giancarlo; Macelloni, Cristina  
PA Nicox S.A., Fr.  
SO PCT Int. Appl., 46 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2004000273   | A1   | 20031231 | WO 2003-EP6496  | 20030620 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| PRAI | IT 2002-MI1392  | A    | 20020625 |                 |          |
| GI   |   |      |          |                 |          |



I

AB The present invention relates to new pharmaceutical compns. for the administration of liquid drugs in solid oral forms, said compns. comprising one or more active ingredients, one or more surface-active agents and optionally a co-surfactant and/or an absorption enhancer absorbed on a solid inert carrier. An emulsion was prepared containing I 100, Cremophor EL 50, Phospholipon 80H 50, Aerosil 200 100, and Explotab 100 g.

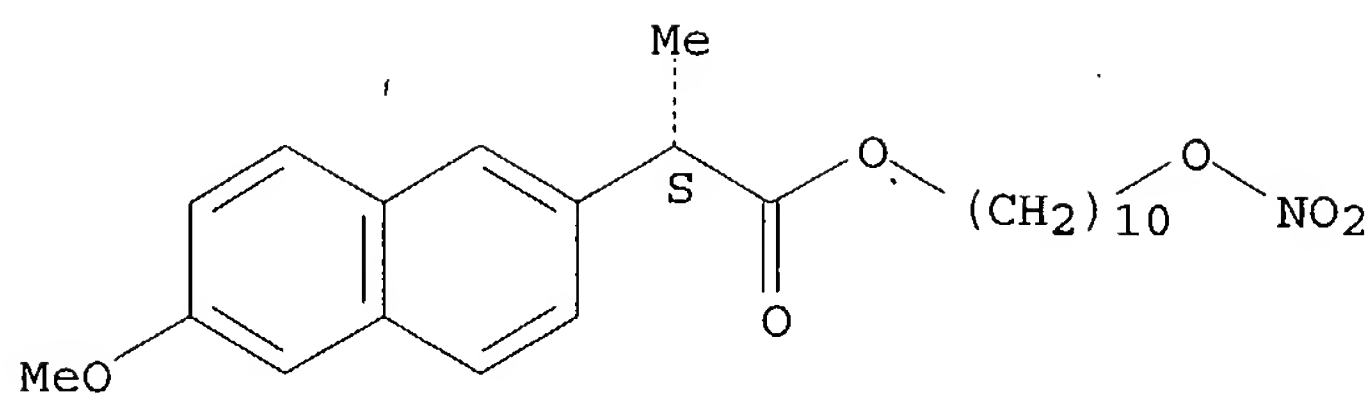
IT 639067-65-5 639067-67-7 639067-69-9  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral pharmaceutical liquid drugs containing nitrate ester NSAIDs having improved bioavailability)

RN 639067-65-5 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- $\alpha$ -methyl-, 10-(nitrooxy)decyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

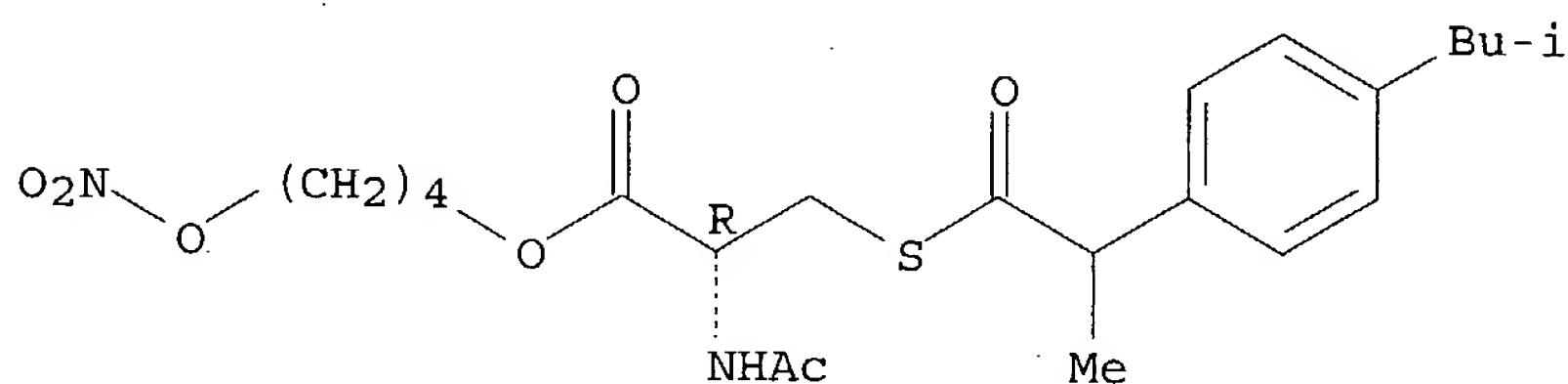
10/612014



RN 639067-67-7 CAPLUS

CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

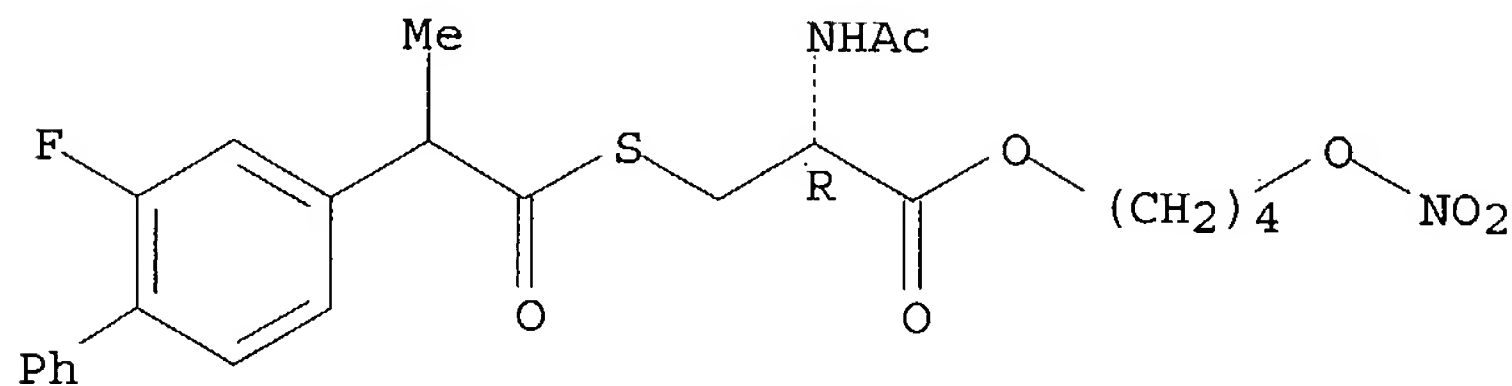
Absolute stereochemistry.



RN 639067-69-9 CAPLUS

CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-fluoro- $\alpha$ -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3

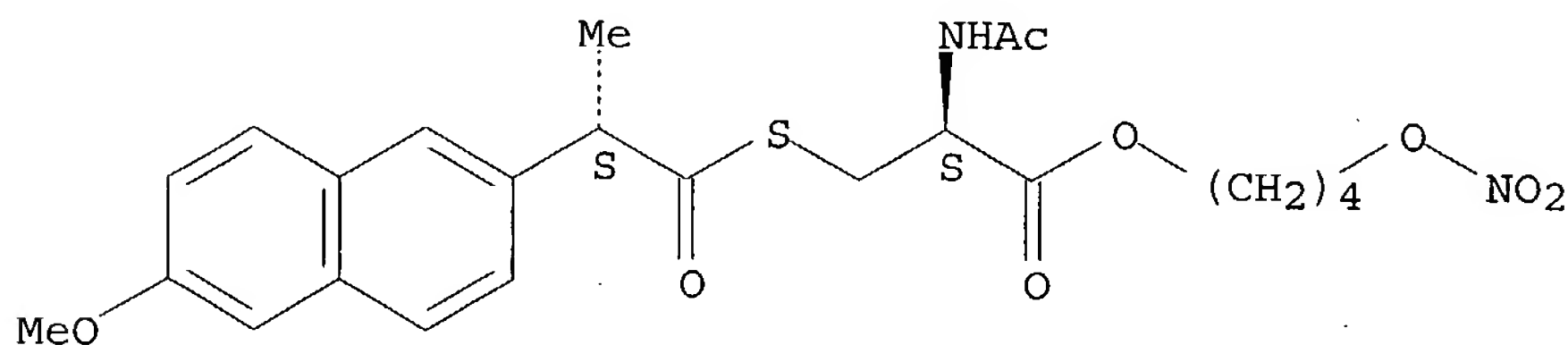
THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/612014

L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:818296 CAPLUS  
DN 139:302040  
TI Nitrooxy derivatives of antiinflammatory/analgesic compounds for the  
treatment of arthritis  
IN Del Soldato, Piero  
PA Nicox S.A., Fr.  
SO PCT Int. Appl., 71 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2003084550   | A1   | 20031016 | WO 2003-EP3183  | 20030327 |
|      | W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, SG, TN, TT, UA, US, UZ, VN, YU, ZA   |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| PRAI | IT 2002-MI773   | A    | 20020411 |                 |          |
| OS   | MARPAT 139:302040   |      |          |                 |          |
| AB   | Antiinflammatory and/or antiinflammatory/analgesic compds. having the formula A(B)b0(C)c0-N(O)s [A contains radical of nonsteroidal antiinflammatory or nonsteroidal antiinflammatory/analgesic drug; B, C = bivalent linking group; s = 1, 2; b0, c0 = 0, 1 (with proviso)], and salts thereof, are disclosed for use in the treatment of arthritis. |      |          |                 |          |
| IT   | 302543-75-5 497818-53-8 612478-28-1<br>RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)<br>(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)   |      |          |                 |          |
| RN   | 302543-75-5 CAPLUS  |      |          |                 |          |
| CN   | D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)  |      |          |                 |          |

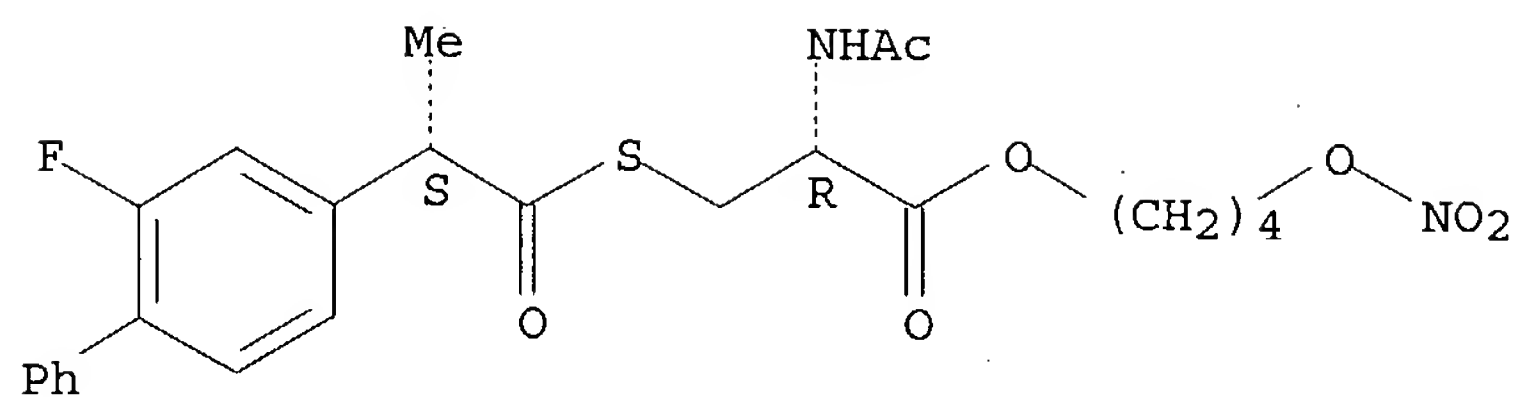
Absolute stereochemistry.



RN 497818-53-8 CAPLUS  
CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-2-fluoro- $\alpha$ -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

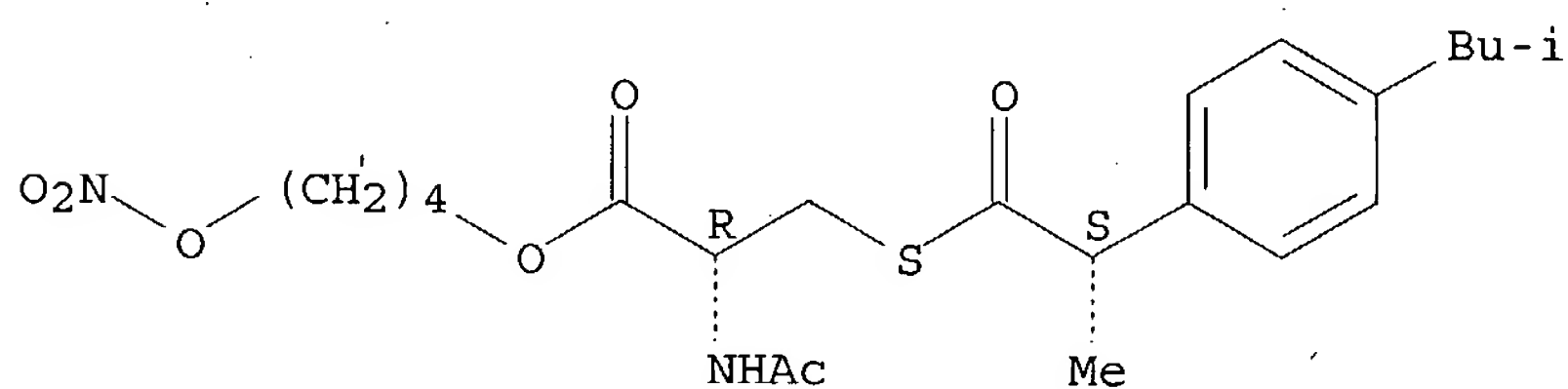
10/612014



RN 612478-28-1 CAPLUS

CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)- $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



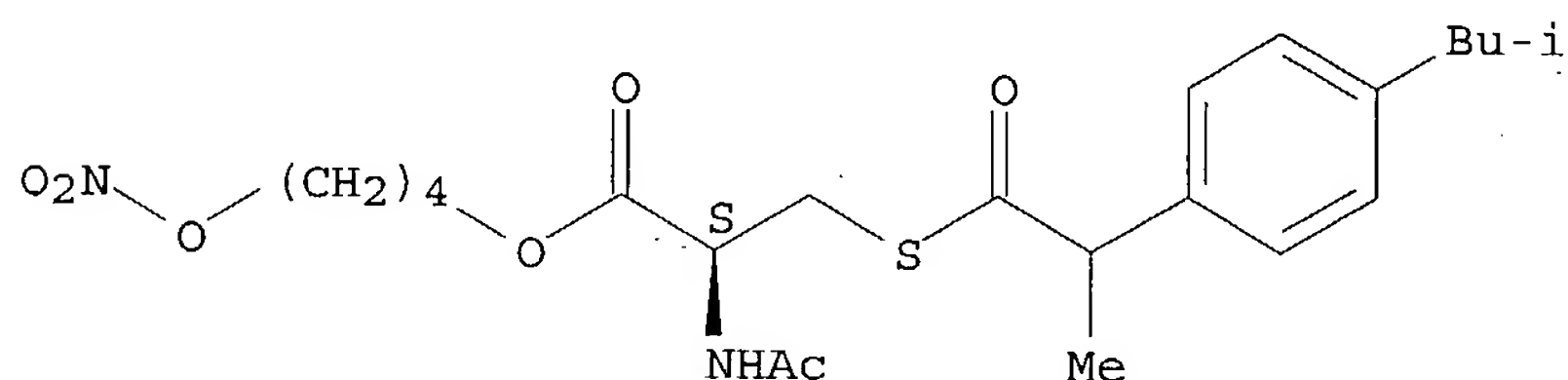
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/612014

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:499717 CAPLUS  
DN 140:314514  
TI Nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibit the growth of various cultured human cancer cells: Evidence of a tissue type-independent effect. [Erratum to document cited in CA138:378736]  
AU Kashfi, Khosrow; Rayyan, Yaser; Qiao, Leon L.; Williams, Jennie L.; Chen, Jie; Del Soldato, Piero; Traganos, Frank; Rigas, Basil  
CS American Health Foundation, Valhalla, NY, USA  
SO Journal of Pharmacology and Experimental Therapeutics (2003), 306(1), 421  
CODEN: JPETAB; ISSN: 0022-3565  
PB American Society for Pharmacology and Experimental Therapeutics  
DT Journal  
LA English  
AB The name of the second author, Yaser Rayyan, was misspelled.  
IT 302543-76-6, NCX 2111  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibition of growth of various cultured human cancer cells and evidence of tissue type-independent effect (Erratum))  
RN 302543-76-6 CAPLUS  
CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



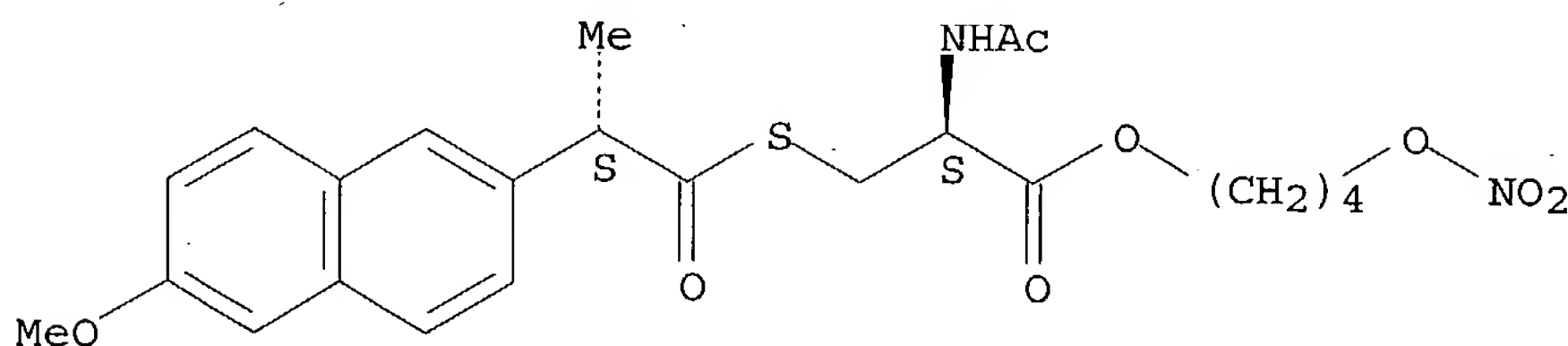
10/612014

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:133017 CAPLUS  
DN 138:163547  
TI Nitrooxy compounds for treatment of vasculopathies  
IN Del Soldato, Piero  
PA Nicox S.A., Fr.  
SO PCT Int. Appl., 26 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.     | KIND   | DATE     | APPLICATION NO. | DATE     |
|------|----------------|--|----------|-----------------|----------|
| PI   | WO 2003013499  | A2   | 20030220 | WO 2002-EP8374  | 20020726 |
|      | WO 2003013499  | A3   | 20031231 |                 |          |
|      | W:             | AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI, SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA             |          |                 |          |
|      | RW:            | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |          |                 |          |
| PRAI | IT 2001-MI1744 | A  | 20010809 |                 |          |

OS MARPAT 138:163547  
AB The invention discloses the use for vasculopathy treatment of nitrooxy compds. (Markush included), or salts thereof. Compds. of the invention include e.g. 2-fluoro- $\alpha$ -methyl-4-diphenylacetic acid (4-nitrooxy)butyl ester (NO-flurbiprofen).  
IT 302543-75-5 497818-53-8  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nitrooxy compds. for treatment of vasculopathies)  
RN 302543-75-5 CAPLUS  
CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)

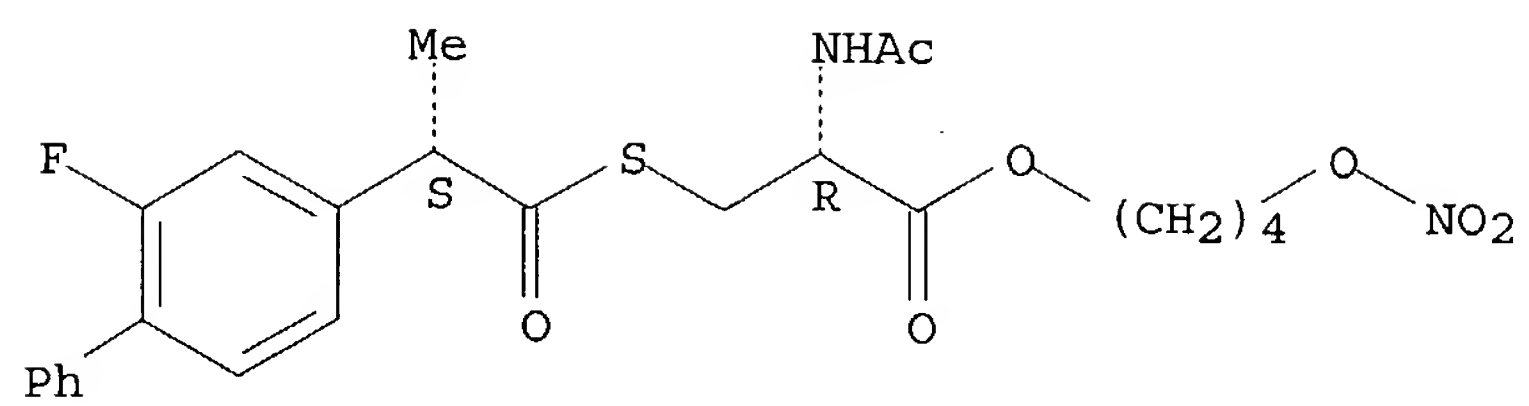
Absolute stereochemistry.



RN 497818-53-8 CAPLUS  
CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-2-fluoro- $\alpha$ -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/612014



10/612014

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:932594 CAPLUS

DN 138:378736

TI Nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibit the growth of various cultured human cancer cells: evidence of a tissue type-independent effect

AU Kashfi, Khosrow; Ryann, Yassir; Qiao, Leon L.; Williams, Jennie L.; Chen, Jie; Del Soldato, Piero; Traganos, Frank; Rigas, Basil

CS American Health Foundation, Valhalla, NY, USA

SO Journal of Pharmacology and Experimental Therapeutics (2002), 303(3), 1273-1282

CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB The novel nitric oxide (NO)-donating nonsteroidal anti-inflammatory drugs (NO-NSAIDs), which are safer than their NSAID counterparts, inhibit the growth of colon cancer cells with far greater potency than traditional NSAIDs. We examined whether NO-NSAIDs inhibit the growth of cancer cells arising from other human tissues. Human pancreatic, colon, prostate, lung, and tongue cancer cell lines were treated with NO-aspirin, -sulindac, -ibuprofen, and -indomethacin or their traditional counterparts. We determined IC50 values, cell proliferation, apoptosis, cell cycle, cyclooxygenase (COX) protein levels, and morphol. changes (light and electron microscopy). All NO-NSAIDs inhibited the growth of all cancer cell lines studied. The potency of NO-NSAIDs was 11- to 6000-fold greater than that of their counterparts (except for the effect of sulindac on lung cancer cells). NO-aspirin was consistently the most potent NO-NSAID in all cell lines tested (except for the lung cancer cell line), sometimes in excess of 100-fold over the other three NO-NSAIDs. NO-NSAIDs inhibited cell proliferation, induced apoptosis, and altered cell cycle phase distribution (G2/M to G0/G1 block). All altered cellular morphol., whereas NO-aspirin induced nuclear disintegration ("atypical" cells) established by electron microscopy. NO-aspirin showed similar effects on two pancreatic cancer cell lines, BxPC-3 (expresses COX) and MIA PaCa-2 (no COX expression), suggesting a COX-independent effect. NO-NSAIDs showed a tissue-type-independent effect. Their pleiotropic effects involve cell renewal, cell death, and cell cycle phase transitions. These results raise the possibility that NO-NSAIDs possess chemopreventive and/or chemotherapeutic activity against a wide variety of human cancers.

IT 302543-76-6, NCX 2111

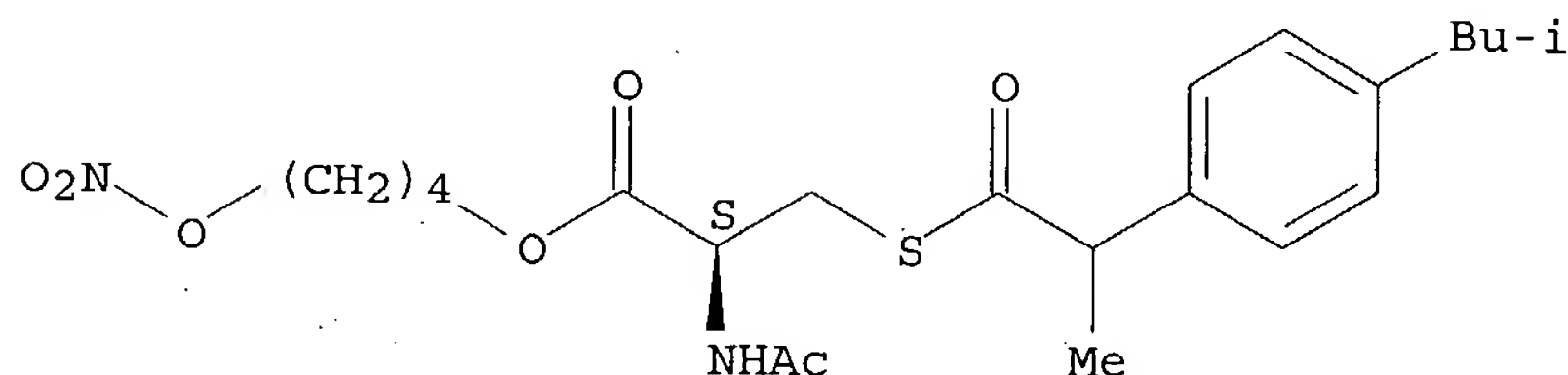
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibition of growth of various cultured human cancer cells and evidence of tissue type-independent effect)

RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/612014

RE.CNT 22      THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/612014

L4 - ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:888544 CAPLUS

DN 137:369833

TI Preparation of nitrooxy cysteine derivatives for the Alzheimer's disease

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 58 pp.

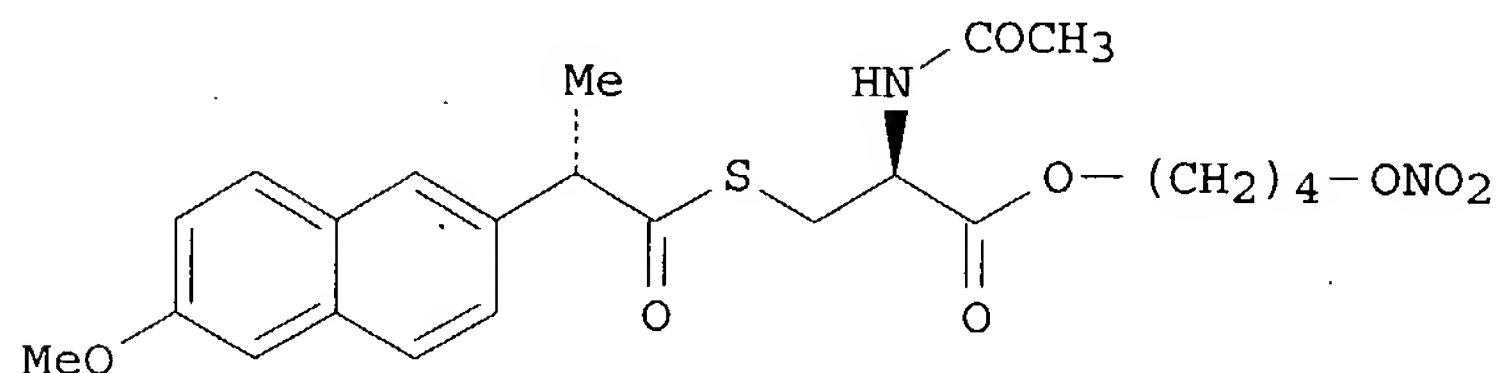
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|      | PATENT NO.        | KIND   | DATE     | APPLICATION NO. | DATE     |
|------|-------------------|--|----------|-----------------|----------|
| PI   | WO 2002092072     | A2   | 20021121 | WO 2002-EP5165  | 20020510 |
|      | WO 2002092072     | A3   | 20030501 |                 |          |
|      | W:                | AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA                 |          |                 |          |
|      | RW:               | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |          |                 |          |
| PRAI | IT 2001-MI985     | A  | 20010515 |                 |          |
| OS   | MARPAT 137:369833 |  |          |                 |          |
| GI   |                   |  |          |                 |          |



II

AB Title compds. A-Bn-Cm-NO<sub>2</sub> [n, m = 0-1 with the proviso that m, n cannot be contemporaneously equal to 0; A = R-T<sub>1</sub>; R = (hetero)cycle; T<sub>1</sub> = (CO)<sup>0-1</sup>, X<sup>0-1</sup>; X = O, S, amino; B = T<sub>2</sub>-X<sub>2</sub>-T<sub>3</sub>; T<sub>2-3</sub> = CO, X, etc.; X<sub>2</sub> = bivalent linking group; C = bivalent linking radical; I] were prepared For instance, 6-methoxy- $\alpha$ -methyl-2-naphthalenacetic acid was coupled to (S)-N-acetylcysteine (DMF/CHCl<sub>3</sub>, CDI, 12 h), the product converted to the 4-bromobutyl ester (THF, Ph<sub>3</sub>P, CBr<sub>4</sub>, 24 h) and that intermediate treated with AgNO<sub>3</sub> (CH<sub>3</sub>CN, reflux, 7 h) to afford II. Nitrooxy derivs. of the invention are effective in inhibiting LPS-induced neurodegeneration and are useful in the treatment of Alzheimer's disease.

IT 302543-75-5P 302543-76-6P 302543-77-7P  
475561-35-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

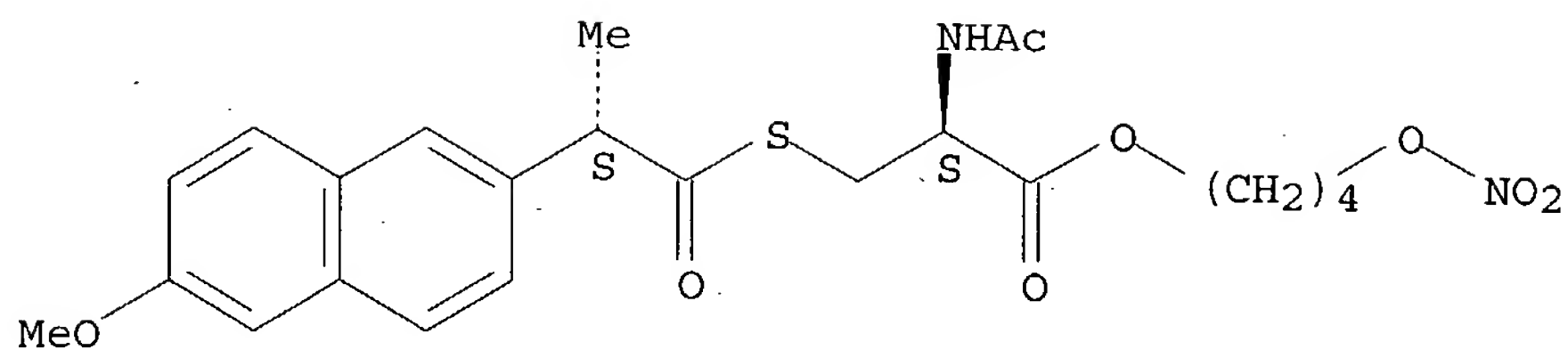
(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

RN 302543-75-5 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

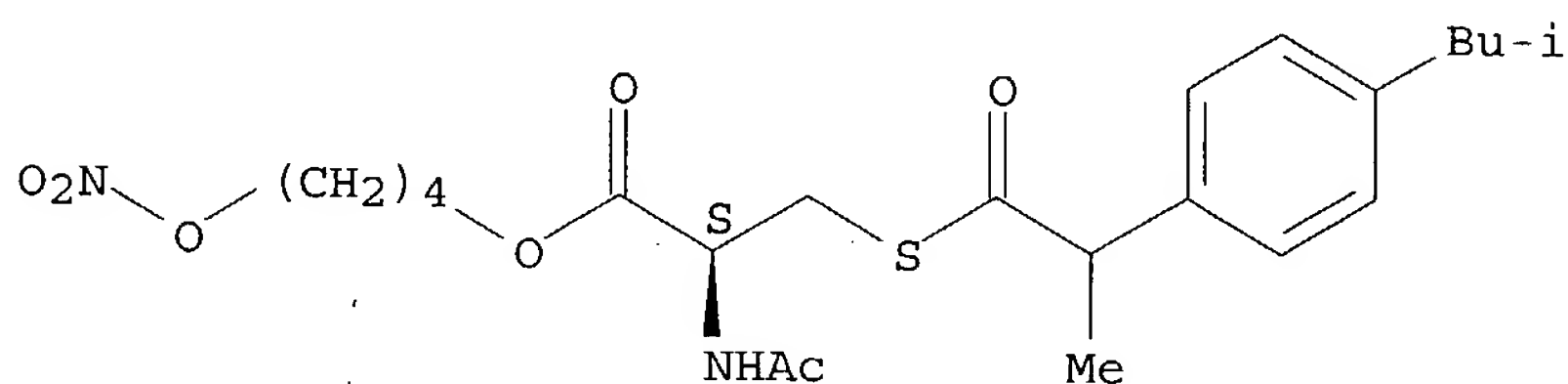
10/612014



RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

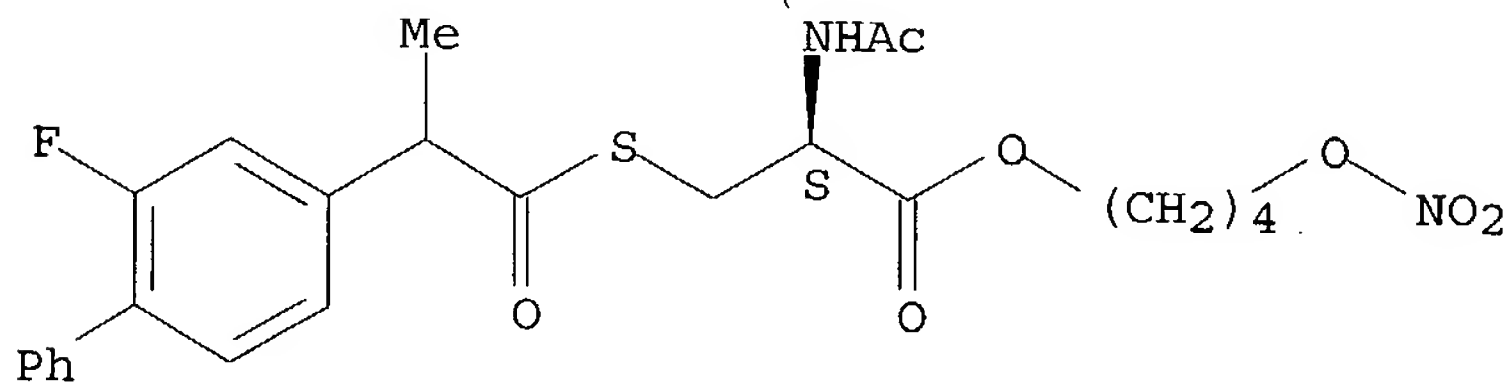
Absolute stereochemistry.



RN 302543-77-7 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-fluoro- $\alpha$ -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

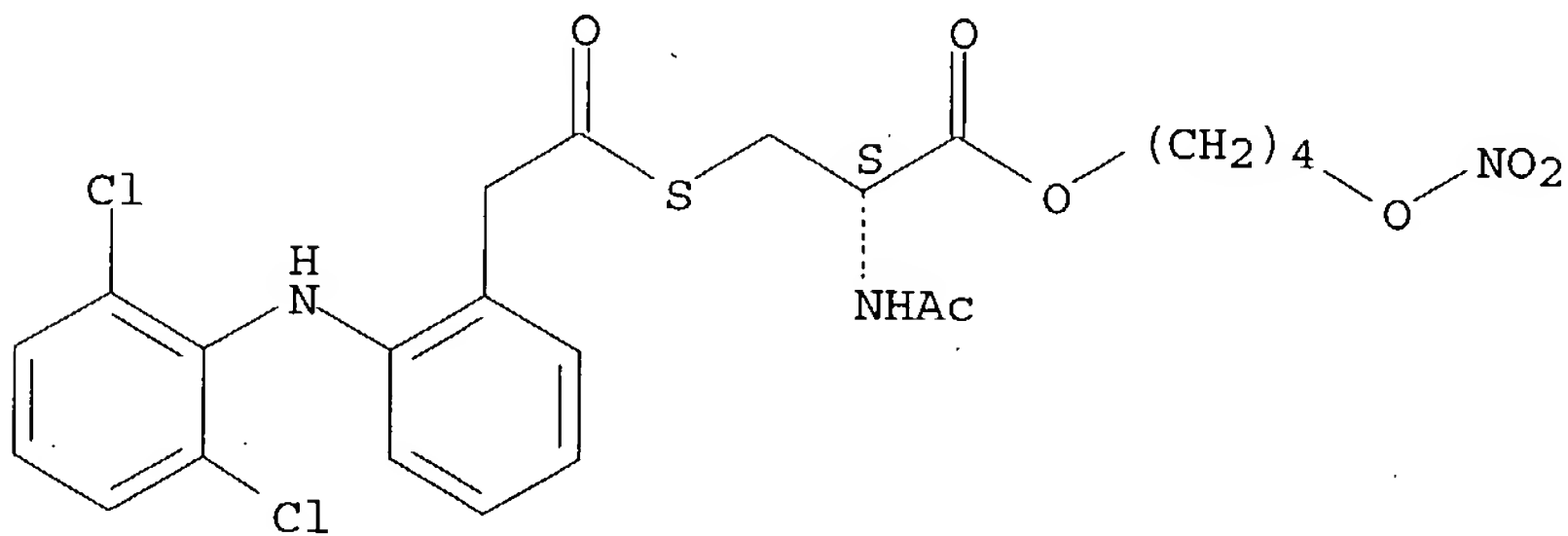
Absolute stereochemistry.



RN 475561-35-4 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-[(2,6-dichlorophenyl)amino]benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/612014

L4 -- ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:293592 CAPLUS

DN 136:325420

TI Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 66 pp.

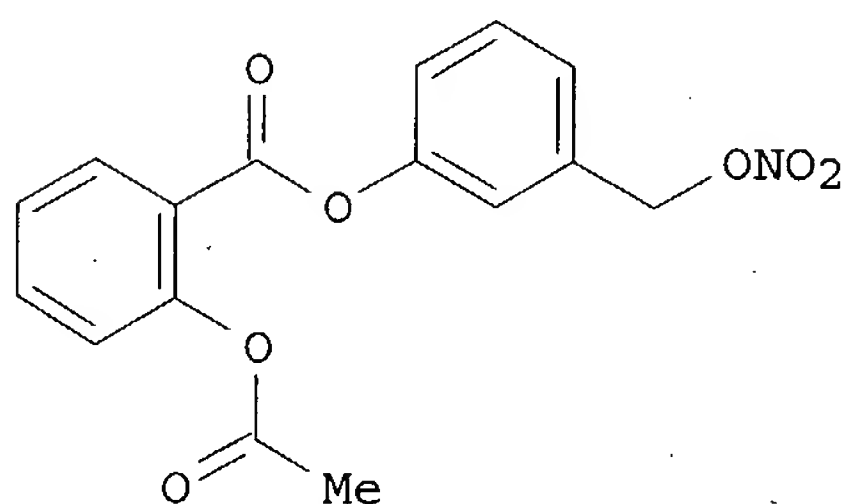
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|      | PATENT NO.        | KIND | DATE     | APPLICATION NO.  | DATE     |
|------|-------------------|------|----------|--|----------|
| PI   | WO 2002030867     | A2   | 20020418 | WO 2001-EP11665  | 20011009 |
|      | WO 2002030867     | A3   | 20020725 |  |          |
|      | W:                |      |          | AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |
|      | RW:               |      |          | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |
|      | IT 1319201        | B1   | 20030926 | IT 2000-MI2201   | 20001012 |
|      | CA 2425655        | AA   | 20020418 | CA 2001-2425655  | 20011009 |
|      | AU 2002014006     | A5   | 20020422 | AU 2002-14006  | 20011009 |
|      | EP 1324974        | A2   | 20030709 | EP 2001-982414   | 20011009 |
|      | R:                |      |          | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |          |
|      | JP 2004511456     | T2   | 20040415 | JP 2002-534256   | 20011009 |
|      | US 2004023890     | A1   | 20040205 | US 2003-398511   | 20030411 |
| PRAI | IT 2000-MI2201    | A    | 20001012 |  |          |
|      | WO 2001-EP11665   | W    | 20011009 |  |          |
| OS   | MARPAT 136:325420 |      |          |  |          |
| GI   |                   |      |          |  |          |



II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies,



10/612014

neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by  $\geq 50\%$  in the oxidative degradation of desoxyribose in aqueous  $\text{Fe}^{2+}(\text{NH}_4)_2(\text{SO}_4)_2$ /thiobarbituric acid solution; and

(test

4): inhibition by  $\geq 50\%$  of DPPH-induced radical production in MeOH solution. For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitration of the resultant Ph ester with  $\text{HNO}_3/\text{H}_2\text{SO}_4$  (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of  $10^{-4}$  M

gave

70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

IT 302543-76-6P

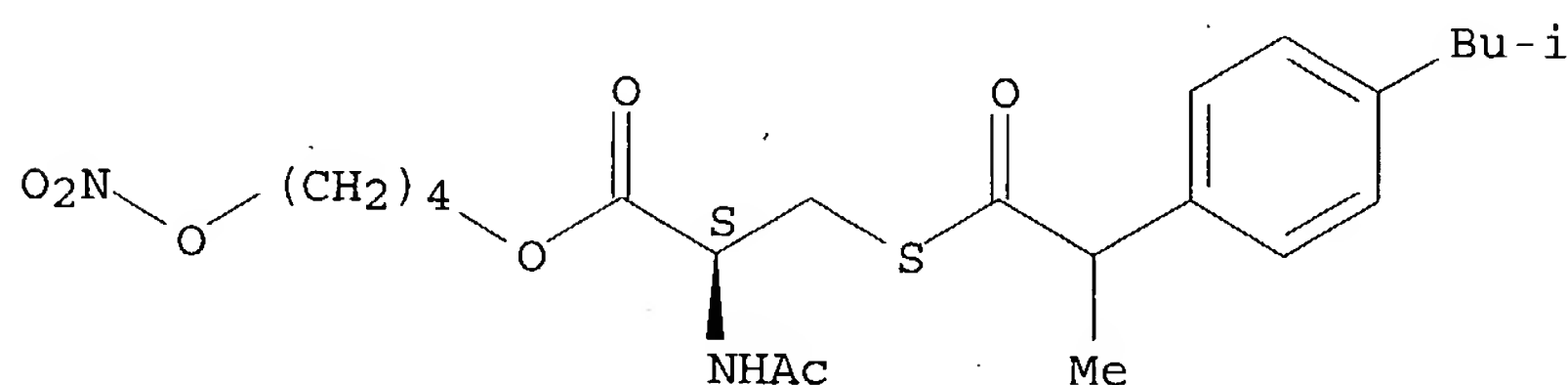
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/612014

L4 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:293591 CAPLUS  
DN 136:309852  
TI Preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs.  
IN Del Soldato, Piero; Benedini, Francesca; Antognazza, Patrizia  
PA Nicox S.A., Fr.  
SO PCT Int. Appl., 72 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2002030866   | A1   | 20020418 | WO 2001-EP11664 | 20011009 |
|      | W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
|      | IT 1319202  | B1   | 20030926 | IT 2000-MI2202  | 20001012 |
|      | CA 2425649  | AA   | 20020418 | CA 2001-2425649 | 20011009 |
|      | AU 2002015932   | A5   | 20020422 | AU 2002-15932   | 20011009 |
|      | EP 1339665  | A1   | 20030903 | EP 2001-986670  | 20011009 |
|      | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |          |
|      | JP 2004511455   | T2   | 20040415 | JP 2002-534255  | 20011009 |
|      | US 2004023933   | A1   | 20040205 | US 2003-398289  | 20030410 |
| PRAI | IT 2000-MI2202  | A    | 20001012 |                 |          |
|      | WO 2001-EP11664   | W    | 20011009 |                 |          |

OS MARPAT 136:309852

AB AX1LWpNO2 [p = 0, 1; A = RT1; R = specified precursor drug radicals; T1 = (CO)t, Xtt; X = O, S, imino, etc.; X1 = TbYTbb; Tb = CO, X; Tbb = (CO)xx, Xxxx; t, tt, xx, xxx = 0, 1; Y, Yt = specified bivalent linker; W = YtO; with provisos], were prepared Thus, acetylsalicylic acid in DMF was treated with NaOEt; after 30 min. the solution was added to a solution of bis(chloromethyl)pyridine (preparation given) in DMF; the mixture was kept 7 days

to give 2-acetyloxybenzoic acid 6-chloromethyl-2-methylpyridinyl ester. The latter was heated with AgNO3 in MeCN at 80° for 30 min. to give 2-acetyloxybenzoic acid 6-nitrooxymethyl-2-methylpyridinyl ester. The latter at 10 µM gave 100% inhibition of HT29 cancer cells.

IT 302543-75-5

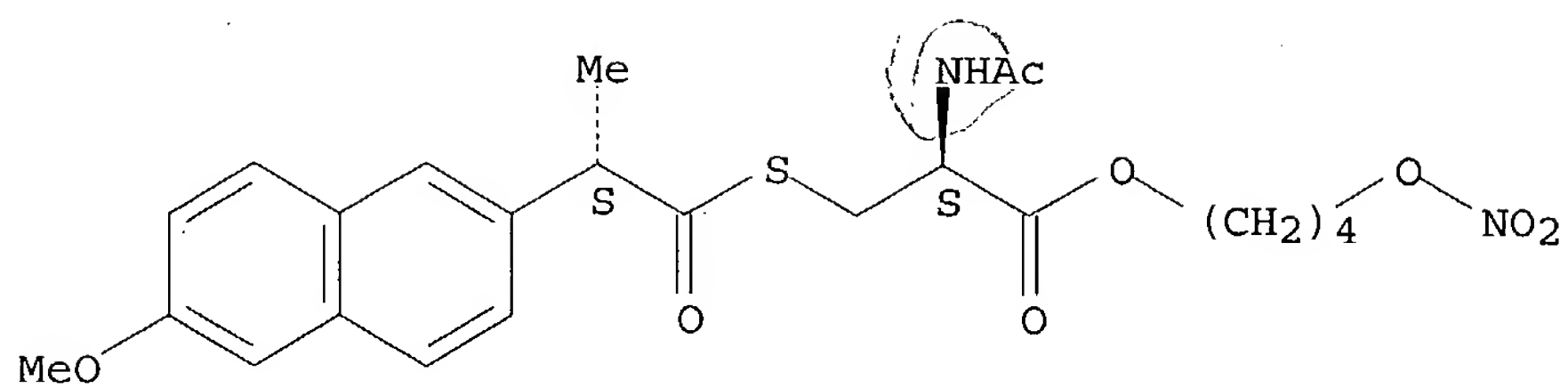
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

RN 302543-75-5 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (αS)-6-methoxy-α-methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/612014



RE.CNT 9      THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/612014

L4 ANSWER 13 OF 14 , CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:742053 CAPLUS

DN 133:310142

TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 159 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|      | PATENT NO.     | KIND   | DATE     | APPLICATION NO. | DATE     |
|------|----------------|--|----------|-----------------|----------|
| PI   | WO 2000061537  | A2   | 20001019 | WO 2000-EP3234  | 20000411 |
|      | WO 2000061537  | A3   | 20010927 |                 |          |
|      | W:             | AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
|      | RW:            | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
|      | IT 1311924     | B1   | 20020320 | IT 1999-MI753   | 19990413 |
|      | CA 2370412     | AA   | 20001019 | CA 2000-2370412 | 20000411 |
|      | BR 2000009702  | A  | 20020108 | BR 2000-9702    | 20000411 |
|      | EP 1169294     | A2   | 20020109 | EP 2000-925203  | 20000411 |
|      | R:             | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |          |                 |          |
|      | JP 2002541233  | T2   | 20021203 | JP 2000-610814  | 20000411 |
|      | NZ 514267      | A  | 20040625 | NZ 2000-514267  | 20000411 |
|      | RU 2237657     | C2   | 20041010 | RU 2001-127576  | 20000411 |
|      | ZA 2001008127  | A  | 20030103 | ZA 2001-8127    | 20011003 |
|      | NO 2001004927  | A  | 20011213 | NO 2001-4927    | 20011010 |
| PRAI | IT 1999-MI753  | A  | 19990413 |                 |          |
|      | WO 2000-EP3234 | W  | 20000411 |                 |          |

OS MARPAT 133:310142

AB Compds. A-B-C-N(O)s and A-C1[N(O)s]-B1 or their salts [s is an integer 1 or 2, preferably s = 2; A is the radical of a drug and is such as to meet the pharmacol. tests reported in the description; C and C1 are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description] were prepared for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy- $\alpha$ -methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.

IT 302543-75-5P, NCX 2101 302543-76-6P, NCX 2111

302543-77-7P, NCX 2131 302543-81-3P, NCX 2136

302543-98-2P, NCX 2061

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

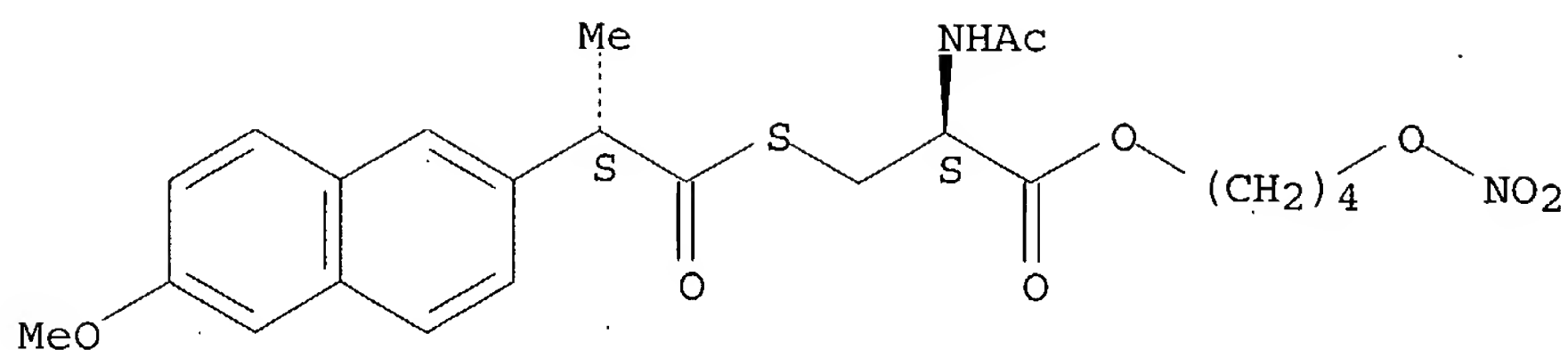
(synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

RN 302543-75-5 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

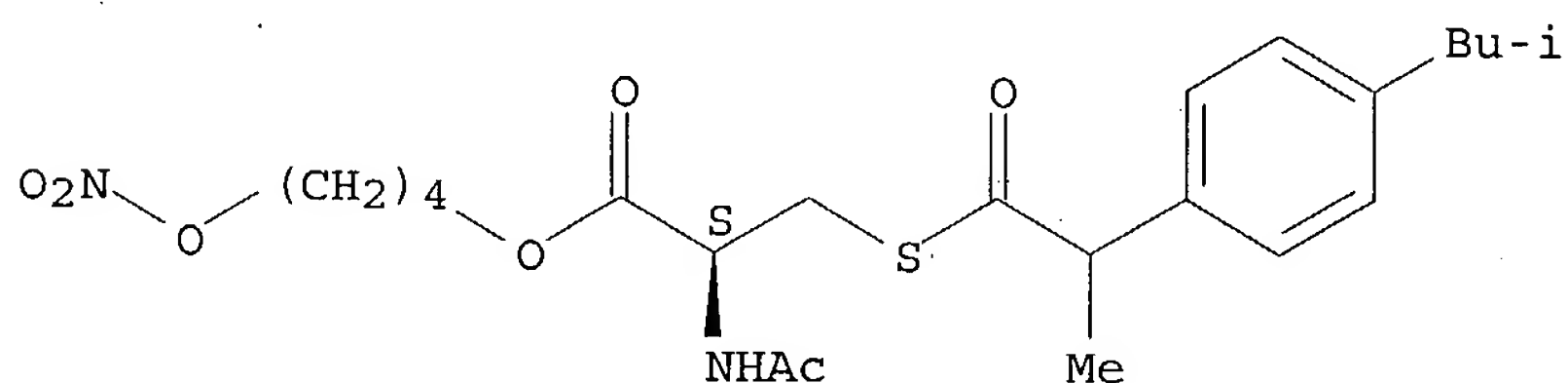
10/612014



RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester,  $\alpha$ -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

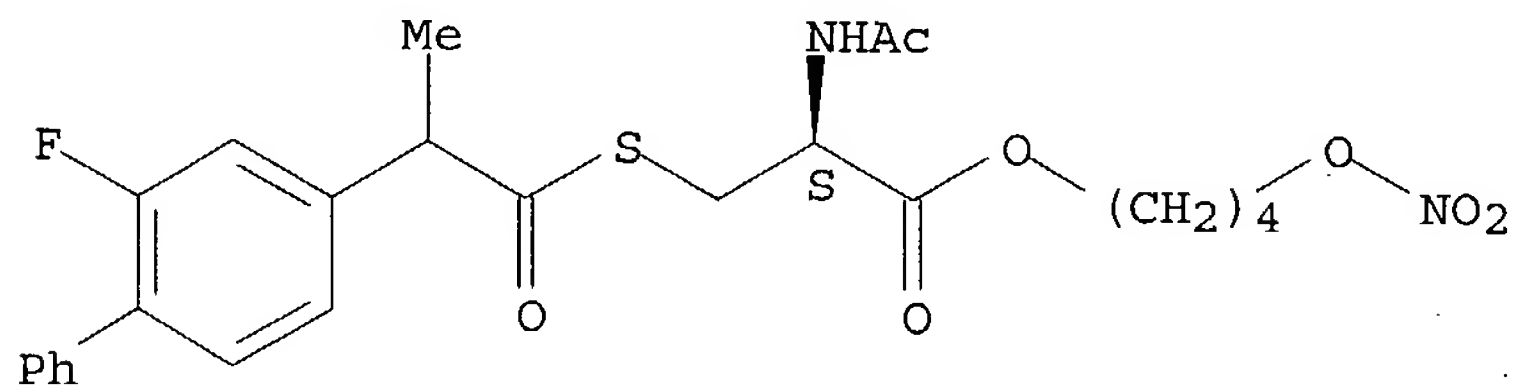
Absolute stereochemistry.



RN 302543-77-7 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-fluoro- $\alpha$ -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

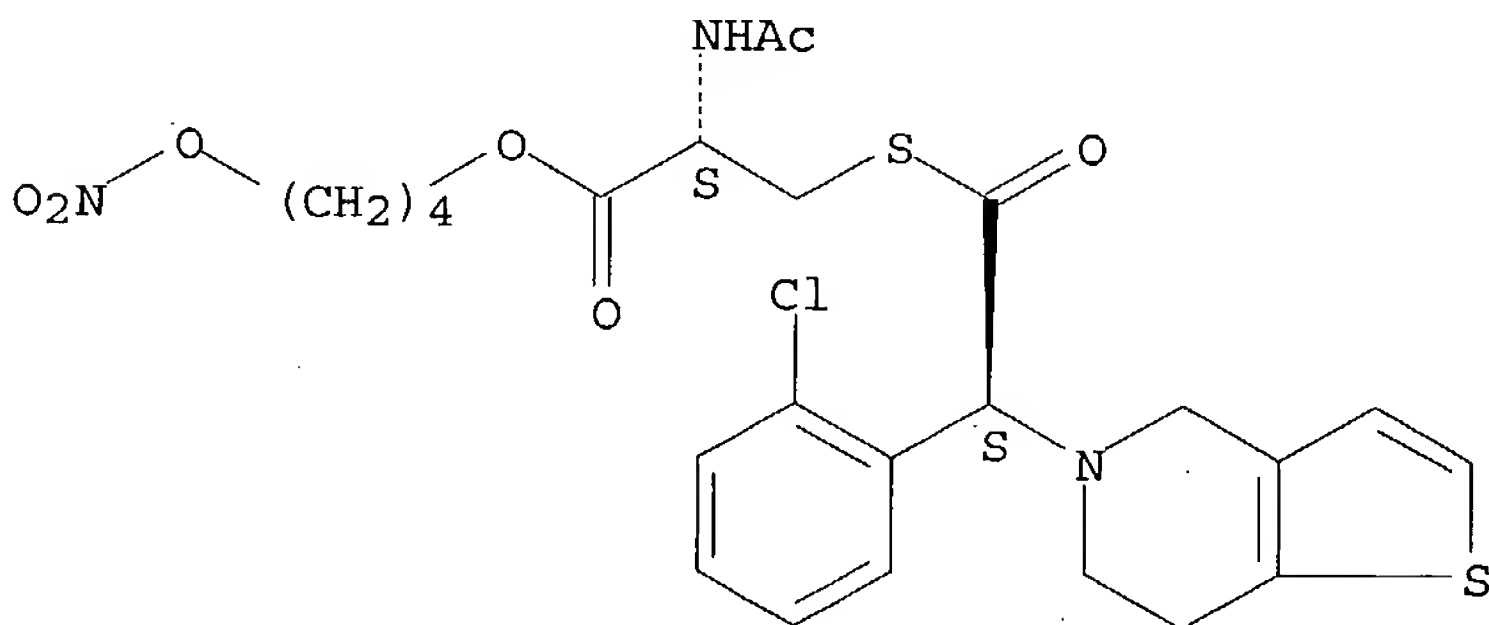
Absolute stereochemistry.



RN 302543-81-3 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, ( $\alpha$ S)- $\alpha$ -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

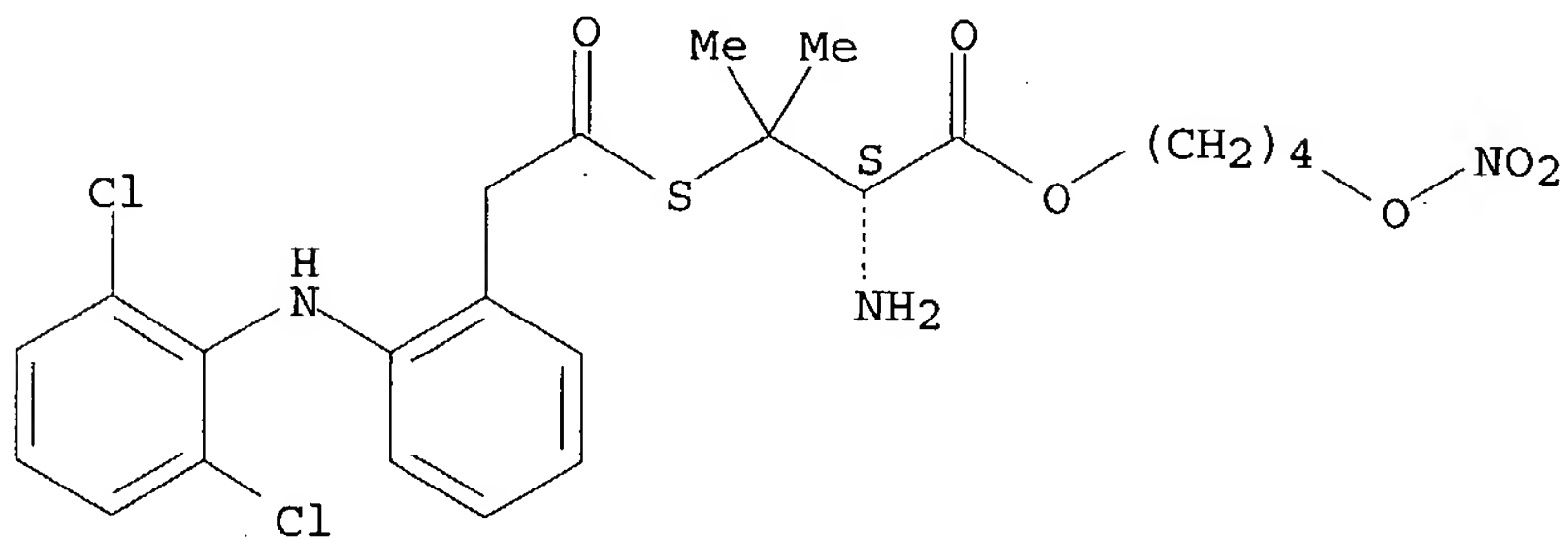


10/612014

RN 302543-98-2 CAPLUS

CN D-Valine, 3-[[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]thio]-,  
4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

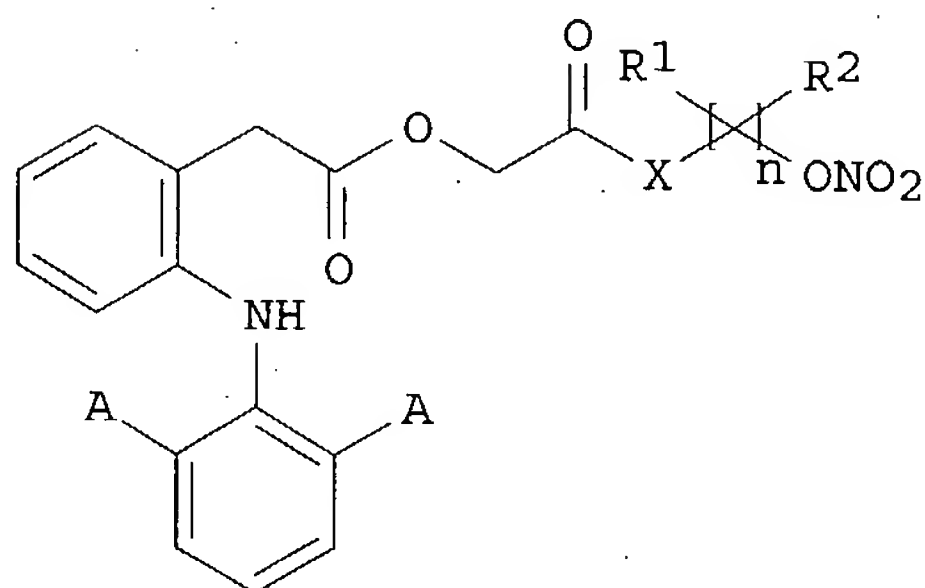
Absolute stereochemistry.



10/612014

L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1996:681459 CAPLUS  
DN 125:328304  
TI Preparation of nitric esters of 2-(2,6-dihalophenylamino)phenylacetoxyacetic acid derivatives  
IN Serra, Masia Xavier; Pi Sallent, Joan  
PA Prodes, S.A., Spain  
SO Eur. Pat. Appl., 16 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | EP 738706   | A1   | 19961023 | EP 1996-106009  | 19960417 |
|      | EP 738706   | B1   | 19981007 |                 |          |
|      | R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |      |          |                 |          |
|      | ES 2092962  | A1   | 19961201 | ES 1995-756     | 19950419 |
|      | ES 2092962  | B1   | 19970716 |                 |          |
|      | AU 9650428  | A1   | 19961031 | AU 1996-50428   | 19960401 |
|      | AU 683790   | B2   | 19971120 |                 |          |
|      | ZA 9602981  | A    | 19961022 | ZA 1996-2981    | 19960415 |
|      | CA 2174287  | AA   | 19961020 | CA 1996-2174287 | 19960416 |
|      | CN 1138027  | A    | 19961218 | CN 1996-105067  | 19960417 |
|      | AT 171936   | E    | 19981015 | AT 1996-106009  | 19960417 |
|      | NO 9601537  | A    | 19961021 | NO 1996-1537    | 19960418 |
|      | JP 09020738   | A2   | 19970121 | JP 1996-98815   | 19960419 |
|      | US 5844696  | A    | 19981201 | US 1996-634763  | 19960419 |
|      | BR 9603235  | A    | 19980428 | BR 1996-3235    | 19960731 |
| PRAI | ES 1995-756   | A    | 19950419 |                 |          |
| OS   | CASREACT 125:328304; MARPAT 125:328304                                    |      |          |                 |          |
| GI   |   |      |          |                 |          |



I

AB The title compds. [I; A = F, Cl, Br; X = O, NH, NR (R = C1-8 alkyl); R1, R2 = C1-8 alkyl, n = 1-10], potentially useful as antiinflammatory agents (no data), were prepared by condensation of 2-(2,6-dihalophenylamino)phenylacetoxyacetic acid with a compound Y-(C)nR1R2ONO2 [Y = OH, NH2, NHR] in the presence of condensing agent such as N,N'-carbonyl diimidazole in an aprotic organic solvent.

IT **183195-07-5P**  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)





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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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COST IN U.S. DOLLARS

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